

A Rare Case Report: Rosai–Dorfman Disease

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Abstract: Sinus histiocytosis with massive lymphadenopathy (SHML) is a benign proliferating histiocytic disorder, predominantly of lymph nodes with extra nodal involvement also seen. We present a case of 15 years old female with history of multiple swellings in neck since 1 month duration. On examination patient had painless bilateral cervical lymphadenopathy. No other ENT manifestations noted. Lymph node biopsy revealed SHML. Abdominal scan and chest X-ray was done which was normal. This case report highlights the clinical, histological aspects of SHML, Rosai–Dorfman disease.

Keywords: Rosai–Dorfman disease, Cervical lymphadenopathy, Sinus histiocytosis

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I. Introduction

Rosai and Dorfman¹ is a distinct benign pseudolymphomatous entity with characteristic histologic features.^{2,3} Most common site for lymphadenopathy is neck. Mediastinal, axillary, inguinal and retroperitoneal nodes may be affected.² The lymphadenopathy when present, tends to be painless and bilateral. Extranodal tissue involvement occurs in 25–40 % of cases and may involve bone, testes, orbit, eyelid, upper respiratory tract, salivary glands, skin, lungs, adnexa, kidney, central nervous system, peritoneum, thyroid, small intestine and joints. Extranodal involvement appears to be more common in patients with immunologic abnormalities which may themselves contribute to poorer prognosis.⁴

The disease is characterized in majority of cases by painless bilateral lymphnode enlargement in the neck, often associated with fever, leucocytosis and polyclonal hypergammaglobulinemia. It presents mainly in the 1st or 2nd decades of life but any age group can be affected especially in extranodal form. SHML should be kept in mind for differential diagnosis of neck masses especially in childhood. The concomitant involvement of one or more sites in the same individual is observed in upto 44.7 % of cases.

Although the geographic distribution is widespread, there has been a high incidence of the disease amongst black African races. Immunohistochemically, the sinus histiocytes are strongly positive for S-100 protein. Immunophenotypic profile suggests, origin from macrophage histiocyte cell types.⁸ The aetiology of the disease include a possible viral infection (Epstein barr virus) and/or an undefined immunological alteration (Table 1).

Table 1

Table 1 Commonest sites of SHML in the head and neck area

Nasal cavity and paranasal sinuses
Orbit
Parotid and submandibular gland
Larynx
Nasopharynx
Temporal bone
Infra temporal fossa
Meninges

II. Case Report

A fifteen years old female patient presented to ENT OPD on February 2016 with history of bilateral multiple bilateral painless swellings in neck of one month duration (Fig. 1). Patient also complained of fever of moderate degree and dry cough since 15 days. Examination of neck revealed on left side revealed enlarged

lymph nodes, level 4; of 5 × 5 cm, level 5; 3 × 3 cm, on right side level 4; of 5 × 3 cm, level 2; 3×3 cm level 5; of 4 × 3 cm, level 5; 3 × 3 cm All the lymph nodes are found to be firm, discrete, non tender and mobile. Examination of ear, nose, oral cavity and oropharynx and larynx revealed normal findings. General physical examination was done and no other group of lymph nodes was found to be enlarged.



Figure 1: 15-year old female presenting with multiple cervical lymphnode enlargement.

Blood examination revealed Hb-13.1 g/dl, RBC- $4.76 \times 10^6/\text{mm}^3$, TLC 9,300 cell/cu mm, ESR-52 mm/h (raised), differential count revealed N76 %, L17 %, E04 %, M3 % Peripheral blood picture revealed normocytic hypochromic anaemia with relative neutrophilia.

FNAC was done and aspiration smears are highly cellular and showed numerous histiocytes arranged in clusters, many of which are seen engulfing mature lymphocytes and neutrophils, plasma cells, plump histiocytes and few atypical giant cells against background of fibrinous tissue, features of sinus histiocytosis. USG neck showed bilateral discrete lymphochoecic areas in level 4, 5 and 6 cervical lymph nodes region suggestive of lymphoma. Chest X-ray and abdominal scan was normal.

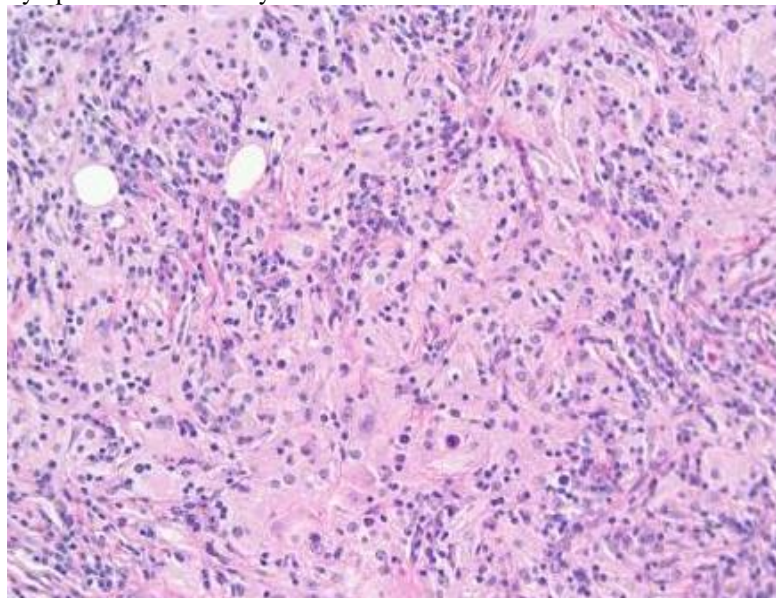


Figure 2: Slide showing aspiration cytology report of R D Disease

III. HISTOPATHOLOGY

Subsequently, the biopsy of one of the cervical lymph node was done. Microscopic examination of the sections cut from paraffin embedded blocks showed fibrous thickening of the lymph node capsule and prominent dilatation of lymph sinuses resulting in partial architecture effacement. The primary lymphoid follicles were present mostly at the cortical areas. The sinuses were occupied by numerous histiocytes having abundant pale cytoplasm and phagocytosed lymphocytes (emperipolesis), plasma cells and occasional neutrophils. Patient was not given any treatment

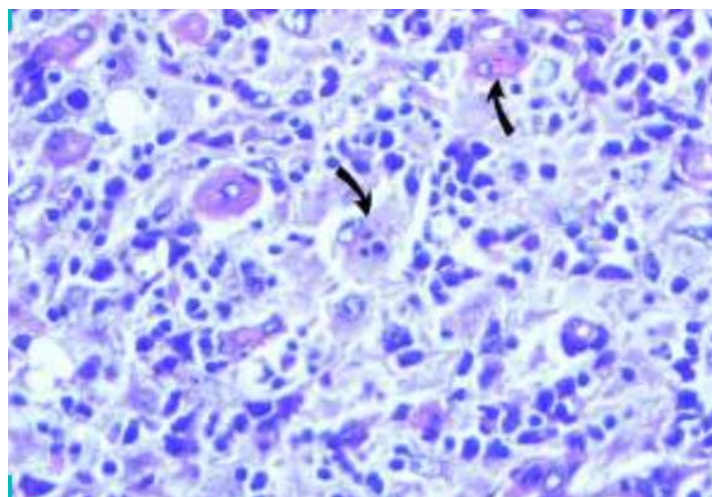


Figure 3: HPE report showing Sinus Histiocytes.

IV. Discussion

SHML or RDD is a rare but well defined, histiocytic proliferative disorder of unknown etiology, characterized frequently by spontaneous remission. Some investigators consider it to be of bone marrow stem cell origin.⁴ It manifests mainly with an asymptomatic cervical lymphadenopathy, occasionally with extranodal locations. Literature reviews show about 600 cases of RDD had been reported till 2004, in all races but mainly in whites (43%), in any age group but mainly in first and second decades (81%), and more in males than females (2:1).⁶ More than 90% of patients with SHML present with massive bilateral mobile and nontender cervical lymphadenopathy. These nodes may at times be matted and prominent by periportal fibrosis. Forty percent of the cases may show extranodal involvement. Low grade fever is generally present along with, normochromic anemia, elevated ESR, leukocytosis and hyperglobulinemia.³ Etiology of this disease is unclear. RDD may be of two types- either familial or infection induced. With respect to the latter, increased antibody titres to Epstein Barr Virus and measles virus have been observed; however etiological evidence is lacking. Immune disturbances are likely to be a feature in some patients. Subtle undefined

Immunological defects are also considered as a casual factor. Human Herpes Virus-6 DNA has been detected in biopsy specimens and is considered as a contributing factor. Also, a familial association has been observed in some cases. It has also been found that stimulation of monocytes/macrophages via macrophage colony stimulating factor (M-CSF) leading to immune suppressive macrophages may be the main pathogenetic mechanism of RDD.⁸ Our case was a young male who presented with multiple cervical and submandibular lymphadenopathy, fever, leukocytosis, and an elevated ESR. However, the possibility of Rosai Dorfman Disease was not considered until FNAC was performed. The cytological features of SHML usually reveal numerous large histiocytes with abundant, pale cytoplasm and phagocytosed lymphocytes (emperipolesis). The background typically shows lymphocytes, plasma cells and occasional neutrophil.⁹ These features were also present in our case. Emperipolesis or lymphophagocytosis is the presence of intact lymphocytes wandering about within the cytoplasm of histiocytes; this is of great diagnostic significance. The internalized lymphocytes are usually located within cytoplasmic vacuoles.¹⁰ The histopathological features include progressive filling up of LN sinuses with normal histiocytes and lymphocytes leading to partial effacement of lymph nodal architecture as seen in our case too. Histiocytes showing similar phenomenon of emperipolesis are present. There may be pericapsular fibrosis and inflammation.⁸ Ultrastructurally, histiocytes lack Birbeck granules and viral particles. On Immunostaining show positivity for S100 protein, CD11C, CD14, CD33 and CD68 antigens and are CD1 negative.⁴ The prognosis is excellent in most cases. Complete spontaneous regression is known to occur. The course of disease however may be protracted over three to nine months. Only two cases of progression, one to malignant lymphoma and another to amyloidosis have been documented.³ Complications are mostly due to pressure effects exerted by the enlarged cervical lymph nodes. The treatment modalities for RDD are nonspecific and include corticosteroids, chemotherapy with a combination of vinca alkaloids and alkylating agents, low dose interferon, antibiotic therapy, radiation therapy and surgical treatment with partial or total resection.⁶ Pathological differential diagnosis of RDD include reactive sinus hyperplasia (in which cells lack emperipolesis and are S100 negative), Langerhans cell histiocytosis (positive for both S100 and CD 1a),

Hodgkin's disease, metastatic carcinoma, malignant melanoma and lymphoma. Perhaps the condition that resembles it most is the sinus histiocytosis induced by cobalt-chromium and titanium that occur in pelvic lymph nodes after hip replacement.⁸ In the case that we observed, most of the histological features were seen

and a conservative approach was followed. After six months of follow up, the patient showed marked regression in the size of the lymph nodes inspite of not being put on any specific treatment. The differential diagnosis of SHML includes Wegener's granulomatosis, midline malignant reticulosis, eosinophil granuloma, Hodgkins disease and fibro inflammatory lesions. Although the extranodal involvement occurs in 40 % of cases painless bilateral cervical Lymphadenopathy is the commonest presentation. Treatment may not be required in majority of patients with SHML since the disease does not usually threaten life or organ function and is often self limited and subject to spontaneous regression.

V. Conclusion

Massive cervical lymphadenopathy is the hallmark of Rosai- Dorfman Disease. Head and neck region is the preferred site of the extranodal form of the disease. The diagnosis of RDD is made on the basis of clinical suspicion, confirmed by cytology and supported by histopathology. Clinicians and pathologists should always be aware of RDD in making a differential diagnosis of cervical lymphadenopathy.

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